

**Amendments to the Specification:**

Please replace the paragraph beginning at page 8, line 7, with the following redlined paragraph:

Figure 12A and 12B illustrate the use of representative ~~flavenoids~~ flavonoids for the treatment of CF patients. Figure 12A shows a recording from a patient with the genotype G551D/ $\Delta$ F508. Amiloride, chloride free solution and isoproterenol were added as indicated. The addition of genistein, as indicated, hyperpolarized nasal PD. Figure 12B is a graph illustrating the average responses of nasal PD to genistein and quercetin of four CF patients with the G551D mutation. The filled bars show, for comparison, the respective responses in healthy subjects.

Please replace the paragraph beginning at page 8, line 14, with the following redlined paragraph:

Figures 13A-13C illustrate the effect of additional representative ~~flavenoids~~ flavonoids and ~~isoflavenoids~~ isoflavonoids on chloride current in epithelial cells. Figure 13A is a graph showing the stimulation of transepithelial chloride currents by resveratrol (100  $\mu$ M), flavanone (100  $\mu$ M), flavone (200  $\mu$ M), apigenin (20  $\mu$ M), apigenin 7-O-neohesperidoside (30  $\mu$ M), kaempferol (20  $\mu$ M), fisetin (100  $\mu$ M), quercetin (30  $\mu$ M), rutin (30  $\mu$ M), genistein (30  $\mu$ M), daidzein (50  $\mu$ M), biochanin A (100  $\mu$ M) and prunetin (100  $\mu$ M) in Calu-3 monolayers. Experiments were performed in the presence of 10  $\mu$ M forskolin. Stimulated currents are plotted relative to forskolin stimulated increase (forskolin stimulated currents are 100%). Figure 13B is a recording showing the effect of 7,4'-Dihydroxyflavone on chloride current in unstimulated tissue. This recording shows a dose-dependent stimulation of transepithelial short-circuit current ( $I_{sc}$ ) across Calu-3 monolayers by 7,4'-Dihydroxyflavone. Increasing concentrations of 7,4'-Dihydroxyflavone (as indicated in  $\mu$ M) were added to mucosal side and dose-dependently stimulated chloride currents. Currents were recorded with a serosal-to-mucosal chloride gradient at 0 mV and pulses were obtained at 2 mV. Figure 13C is a recording illustrating the effect of trimethoxy-apigenin. This recording shows dose-dependent stimulation of transepithelial short-circuit current ( $I_{sc}$ )

across Calu-3 monolayers by trimethoxy-apigenin. Increasing concentrations of trimethoxy-apigenin (as indicated in  $\mu\text{M}$ ) were added to mucosal side and dose-dependently stimulated chloride currents. Experiment was performed on unstimulated tissue. Currents were recorded with a serosal-to-mucosal chloride gradient at 0 mV and pulses were obtained at 2 mV.

Please replace the paragraph beginning at page 19, line 10, with the following redlined paragraph:

Within certain preferred embodiments, ascorbic acid or a derivative thereof is used in combination with a polyphenolic compound as described above. Certain representative combinations include ascorbic acid and one or more ~~flavenoids~~-flavonoids and/or ~~isoflavenoids~~-isoflavonoids (such as genistein and ascorbic acid; and kaempferol and ascorbic acid). Ascorbic acid may generally be used to treat or prevent genetic loss of chloride secretory function (*e.g.*, cystic fibrosis), as well as other related loss or reduced chloride secretory function (*e.g.*, intestinal constipation, dry eye syndrome and obstructive airway diseases).

Please replace the paragraph beginning at page 26, line 24, with the following redlined paragraph:

These results show that the representative ~~flavenoids~~-flavonoids quercetin, apigenin, kaempferol and biochanin A stimulate chloride transport across epithelial tissues derived from the airways *in vitro*, and across nasal epithelium *in vivo*. The results also show that the CFTR mutants  $\Delta\text{F508}$  and G551D can be activated by the representative compounds genistein and apigenin.

Please replace the paragraph beginning at page 29, line 9, with the following redlined paragraph:

This Example illustrates the effect of further ~~flavenoids~~-flavonoids and ~~isoflavenoids~~-isoflavonoids on chloride currents in airway epithelial cells.